Paper 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ALAN A. RUBIN

Appeal 2001-1035
Application 08/835,482[1]

Before: WILLIAM F. SMITH, Administrative Patent Judge, and McKELVEY, Senior Administrative Patent Judge, and POTEATE, Administrative Patent Judge.

McKELVEY, Senior Administrative Patent Judge.

Decision on appeal under 35 U.S.C. § 134

The appeal is from a decision of a primary examiner rejecting claims 1 and 11-12. We affirm.

A. Findings of fact

The record supports the following findings by at least a preponderance of the evidence.[2]

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[1] Application for patent filed 8 April 1997. The named inventor is the real party in interest (Paper 20, Supplemental Appeal Brief, page 1).

[2] To the extent these findings of fact discuss legal issues, they may be treated as conclusions of law.

The invention

1. In the "Background and Prior Art" portion of the specification, we are told that (page 1, lines 18 to page 2, line 12)(matter in [brackets] added):

> Parkinson's disease is associated with the depletion of dopamine[3] from cells in the corpus striatum. Since dopamine does not cross the blood brain barrier and cannot therefore be used to treat Parkinson's disease, its immediate precursor, levodopa,[4] is used instead because it penetrates the brain where it is decarboxylated[5] to dopamine. But levodopa is also decarboxylated to dopamine in peripheral tissues and consequently only a small portion of administered levodopa is transported unchanged to the brain. This reaction can be blocked by carbidopa[6] which inhibits decarboxylation of peripheral levodopa but cannot itself cross the blood brain barrier and has no effect on the metabolism of levodopa in the brain.
>
> The combination of carbidopa and levodopa is considered to be the most effective treatment for symptoms of Parkinson's disease (The Medical Letter, 35:31-34, 1993 [copy in the record]). Nevertheless, certain limitations become apparent within two to five years of initiating combination therapy. As the disease progresses, the benefit from each dose becomes short ("the wearing off effect") and

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[3] The formula of dopamine is shown in entry 3479 from The Merck Index, CD-ROM, Version 12:1a, ISSN 1359-2947 (12th ed. 1996). A copy of the entry is found in an Appendix attached to our opinion.

[4] The formula of levodopa is shown in entry 5490 from The Merck Index, CD-ROM, Version 12:1a, ISSN 1359-2947 (12th ed. 1996). A copy of the entry is found in an Appendix attached to our opinion.

[5] Decarboxylate means remove a —COOH group.

[6] The formula of carbidopa is shown in entry 1843 from The Merck Index, CD-ROM, Version 12:1a, ISSN 1359-2947 (12th ed. 1996). A copy of the entry is found in an Appendix attached to our opinion.

some patients fluctuate unpredictably between mobility and immobility ("the on-off effect"). "On" periods are usually associated with high plasma levodopa concentrations and often include abnormal involuntary movements, i.e., dyskinesias. "Off" periods have been correlated with low plasma levodopa and bradykinetic episodes.

In an effort to reduce the occurrence of "wearing off" and "on-off" phenomena, a controlled release oral dosage combination was introduced with claims of slow and simultaneous release of carbidopa and levodopa from the formulation (US Patent Number 4,900,755 issued February 13, 1990). Data from clinical trials cited in the patent indicate that effective antiparkinson effects were achieved with fewer daily doses of the controlled release form as compared with the conventional combination.

2. The specification goes on to say (page 2, lines 12-22):

Nevertheless, there remains a significant flaw in the therapeutic application of controlled release carbidopa-levodopa; that is the considerable delay in onset of action. Mean time to peak concentration in healthy elderly subjects was found to be two hours for controlled release carbidopa-levodopa and only 0.5 hours for the conventional form (Physicians Desk Ref., 47th Ed., p. 976, 1993 [copy in the record]). A controlled release dosage form that could also provide rapid onset of action, at least equivalent to that of conventional carbidopa-levodopa would have an obvious clinical advantage over current therapy.

3. The "purpose and principal object" of the invention is (specification, page 2, lines 33-38):

> to provide an improved method for the treatment of Parkinson's disease by using novel formulations of the combination carbidopa-levodopa which a) are effective in preventing the symptoms of Parkinson's disease and yet which b) act rapidly avoiding significant onset delay common to the standard controlled release therapy.

4. The formulations of the invention have (1) an immediate release component and (2) a controlled (or delayed) release component (specification, page 3, lines 2-4). The nature of the invention is described as following in the specification (page 3, lines 2-9):

> The novel oral dosage formulations of the present invention each contain immediate release and controlled release components of the antiparkinson agents carbidopa (5-200 mg) and levodopa (25-600 mg). The conventional immediate release combination of carbidopa-levodopa reaches peak plasma concentrations in 30 minutes whereas the onset of the controlled release component is two hours followed by prolonged release over a four- to six-hour period.

5. According to applicant (specification, page 3, lines 10-16):

> The usual daily therapeutic dose of levodopa, when administered with carbidopa, is 300-750 mg and the dose of carbidopa approximately 75 mg per day but the latter is apparently devoid of adverse effects even at doses of 400 mg per day ***.

6. Applicant acknowledges, however, that "the optimum daily dosage of carbidopa-levodopa must ultimately be determined by titrating each patient ***" (specification, page 3, lines 15-16).

The claims

7. Claims 1 and 11-12 are on appeal.

8. In his Supplemental Appeal Brief (Paper 20), applicant does not single out dependent claims 11-12 for separate consideration.

9. Accordingly, claims 1 and 11-12 stand or fall together and we consider the appeal on the basis of claim 1. 37 CFR § 1.192(c)(7).

10. Claim 1 reads (indentation and matter in [brackets] added):

> A method for treating Parkinson's disease using an oral dosage formulation comprising
>
> [1] an immediate release layer of 10-25 mg of carbidopa and 50-200 mg of levodopa and
>
> [2] a sustained release layer of 25-75 mg of carbidopa and 100-400 mg of levodopa
>
> whereby, following administration, carbidopa and levodopa are available for rapid and sustained therapeutic action.

The examiner's rejection

11. The examiner has rejected claims 1 and 11-12 "as being unpatentable over the combined teachings" of (1) Dempski,

U.S. Patent 4,900,755 (1990)[7] and (2) Conte, U.S. Patent 5,738,874 (1998, filed 24 March 1995).[8]

Dempski

12. Dempski describes an invention which (col. 1, lines 12-17):

> is concerned with a controlled release formulation for the simultaneous delivery of levodopa and carbidopa in the treatment of parkinsonism whereby the adverse reactions and inadequacies often experienced with the administration of standard carbidopa/levodopa combinations are minimized.

13. One carbidopa/levodopa formulation which Dempski says is "easier to use" (Formulation No. 3) is described in Example 4 (col. 4, lines 48-62; col. 6, line 47 and 53-54).

14. Example 4 describes a formulation containing carbidopa and levodopa (col. 4, lines 52-53) as well as other ingredients needed to cause the formulation to be a controlled release formulation.

15. According to Dempski, appropriate dosages are (col. 3, lines 51-52):

Levodopa 20-1200 mg Carbidopa 5-300 mg

Preferred dosages are (id.; see also Dempski claim 1):

Levodopa 100-400 mg Carbidopa 25-100 mg.

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[7] Dempski is prior art under 35 U.S.C. § 102(b).

[8] Conte is prior art under 35 U.S.C. § 102(e). Applicant has not attempted to antedate Conte (37 CFR § 1.131). In this respect, we note that Conte is said to be based on a PCT application which is said to have been published on 31 March 1994. The published PCT application would be prior art under 35 U.S.C. § 102(b).

16. An understanding of the manner in which controlled release is accomplished is readily apparent from Figs. 1, 2, 3 and 3a:

FIG. 1

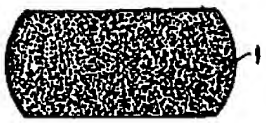


FIG. 2

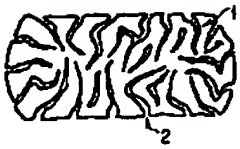


FIG. 3

FIG. 3a

17. Fig. 1 "is a cross-section of a tablet-shaped homogeneous polymer matrix showing the drug components, **1**, homogeneously dispersed in the matrix." Col. 2, lines 66-68.

18. Fig. 2 "is a schematic representation of the same polymer matrix, **1**, after some of the drug has been delivered by diffusion by entry of liquids into the tortuous microporous channels, **2**, followed by exit of drug solution through the same tortuous path. This matrix remains essentially intact while delivering its drug content." Col. 3, lines 1-7.

19. Fig. 3 "is a cross-section of a schematic representation of the polymer matrix, **1**, after some of the drug has been delivered by erosion by liquids whereby polymer, **1**, and active ingredients, **2**, are dispersed in the fluid as solute or suspensoid." Col. 3, lines 8-12.

20. Fig. 3a "is a schematic representation of the polymer matrix, **1**, after essentially all of the drug, **2**, has been delivered by erosion. This matrix completely disintegrates while delivering its drug content." Col. 3, lines 13-16.

Difference between claim 1 and Dempski

21. Dempski differs from the subject matter of claim 1 in that claim 1 calls for a two-layer release mechanism, one layer being an immediate release layer and the other layer being a sustained release layer.

Conte

22. In the "Prior Art" section of Conte, we find the following discussion concerning the administration of L-dopa, another name for levodopa (col. 2, beginning at line 42):

> A typical example is L-dopa used in treating Parkinson's disease. In the organism, L-dopa is metabolized to dopamine, which is the drug active ingredient. However, only the unmodified form, i.e., L-dopa, is capable of crossing the blood-brain barrier.
>
> L-dopa is rapidly absorbed into the gastroenteric tract and spreads out in the various organs and tissues, including the CNS [central nervous system]. L-dopa has plasmatic

half-life of approx. 1 hr and is converted into dopamine mainly by decarboxylation.

L-dopa is rapidly decarboxylated to dopamine also in the gastroenteric tract; hence, the quantity of L-dopa reaching the CNS is extremely low. Furthermore, the presence of excess dopamine deriving from peripheral decarboxylation in organs external to the CNS may produce massive side effects.

Should drugs inhibiting peripheral decarboxylation, such as *** carbidopa, be administered with or before L-dopa administration, the peripheral conversion of L-dopa into dopamine would be drastically reduced and higher amounts of L-dopa would reach the systemic circulation and the brain, where conversion into dopamine produces the desired therapeutic effect. Thus, much lower L-dopa doses can have a high therapeutic effect and, at the same time, produce lesser side effects.

In such complex pathological situations, the availability of pharmaceutical compositions capable of liberating different drugs at successive times would solve a therapeutic problem also involving a serious social impact, the treatments being mainly addressed to elderly persons.

23. Conte describes a tablet which is capable of overcoming prior art problems (col. 3, lines 8-9) and involves a device for releasing drugs at different rates (col. 3, lines 35-36).

24. The tablet is said to consist of (col. 3, lines 38-46):

(1) a first layer containing one or more drugs with immediate or controlled release formulation;

(2) a second layer containing one or more drugs with slow release formulation and

(3) a third layer, which is characterized as being a low-permeability barrier coating.

25. The drugs in the second layer may be the same as or different than the drugs in the first layer.

26. One preferred embodiment is shown in Fig. 2, where **4** is the immediate or controlled release layer (1), **5** is the slow release layer (2) and **6** is the barrier-type layer (3):

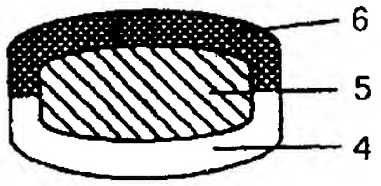


FIG. 2

27. From claim 6 of Conte (col. 18), it is apparent that two drugs contemplated for use in the Conte system are L-dopa and carbidopa.

B. Discussion

1. Prima facie obviousness

The examiner's prima facie case of obviousness is supported by substantial evidence in the form of Dempski and Conte.

Dempski tells us that one having ordinary skill in the art knew that levodopa and carbidopa could be administered

simultaneously for the purpose of treating Parkinson's disease. It turns out, however, that a single dose of both compounds had problems. Accordingly, Dempski determined that the compounds should be administered in the form of a controlled slow release mechanism. Indeed, applicant concedes that "[t]he examiner correctly states *** that 'the combination of levodopa and carbidopa in a sustained release formulation is well known in the art.'" Supplemental Appeal Brief, page 2. The Dempski slow release mechanism is a "single" layer.

Dempski differs from the subject matter of claim 1 in that claim 1 calls for a two-layer release mechanism, one layer being an immediate release layer and the other layer being a sustained release layer (Finding 21).

Conte, while directed to the administration of drugs in general, including mixtures of levodopa and carbidopa, describes a device containing first and second drug layers in which the first layer involves immediate or controlled release of a drug and the second layer involves slow release of the same or a different drug. The Conte device is said to overcome problems (col. 2, line 42 through col. 3, line 3) with devices which release drugs at a constant rate (col. 3, lines 8-9). Applicant concedes that the examiner correctly determined that "the prior art teaches formulation comprising multiple release layers to provide for immediate and sustained release of actives, including levodopa and carbidopa". Supplemental Appeal Brief, page 3.

One skilled in the art armed with Conte would have been aware of problems associated with the Dempski manner of administration of drugs. Conte describes Dempski's problem, as well as its solution. Furthermore, Conte explicitly describes solution of Dempski's problem with respect to administration of levodopa and carbidopa, the dosages suggested by Dempski, to treat Parkinson's disease. Hence, Conte provides a reason, suggestion, teaching, incentive or motivation to replace the Dempski device with the Conte device. Insofar as we can tell, applicant has done exactly what Conte teaches. In other words, applicants have used a known technique in a known manner to address a known problem to obtain an entirely expected result. Cf. In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1889 (Fed. Cir. 1991) (the claim elements appear in the prior art in the same configurations, serving the same functions, to achieve the results suggested in the prior art).

2. Applicant's arguments

A first argument made by applicant is interesting. The argument seems to be that the prior art acknowledged by Conte or cited against Conte, establishes that Conte must have discovered something different from what Conte says he discovered (Supplemental Appeal Brief, pages 3-4). Unfortunately for applicant it does not matter whether Conte correctly understood the precise point of "novelty" of his invention. We are not here to resolve the patentability of the Conte invention; rather, we

are here to resolve the patentability of applicant's claimed invention in light of what is described by Dempski and Conte.

A second argument made by applicant is that Conte does not describe the dosages set out in applicant's claim 1 (Supplemental Appeal Brief, page 4). In making the argument, applicants apparently overlook the dosages described by Dempski. See Finding 15. Clearly, one skilled in the art charged with knowledge of both Dempski and Conte would have immediately appreciated the fact that the overall dosages described by Dempski would be used in divided form in the Conte environment. Applicant cannot avoid the force of the examiner's obviousness position by discussing only Conte and playing ostrich with Dempski. In re Keller, 642 F.2d 413, 426, 208 USPQ 871, 882 (CCPA 1981) (one cannot show nonobviousness by attacking individual references where a combination of references is used to support rejection); In re Young, 403 F.2d 754, 757, 159 USPQ 725, 728 (CCPA 1968) (obviousness rejection cannot be overcome by attacking references individually).

A third argument seems to be that the Conte layers "comprise a sustained release core of carbidopa-levodopa overcoated only with an immediate release layer" (Supplemental Appeal Brief, paragraph bridging pages 4-5 (emphasis in original)). We concede to having some difficulty understanding the precise point trying to be made. However, nothing has been called to our attention which would demonstrate that the "immediate release layer" of

claim 1 differs from Conte's first layer or that the "sustained release layer" of claim 1 differs from Conte's second layer.

A fourth argument is that Conte also describes the use of a third layer and that applicant does not require Conte's third layer. The problem with applicant's argument is that its claimed formulation "comprises" a first and second layer. Accordingly, applicant's claim 1 does not exclude the presence of a third layer, such as Conte's third layer. Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 1271, 229 USPQ 805, 812 (Fed. Cir. 1986) (phrase "comprising" is a term of art which does not exclude additional unrecited elements); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 802 (CCPA 1981) ("comprising" leaves claim open to the inclusion of any and all additional steps).

C. Order

Upon consideration of the appeal, and for the reasons given, it is

ORDERED that the examiner's rejection of claims 1 and 11-12 as being unpatentable under 35 U.S.C. § 103(a) over Dempski and Conte is affirmed.

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED.

WILLIAM F. SMITH
Administrative Patent Judge

FRED E. McKELVEY, Senior
Administrative Patent Judge

LINDA R. POTEATE
Administrative Patent Judge

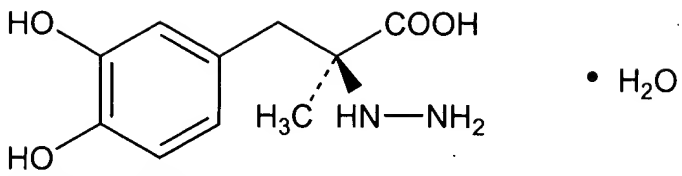
BOARD OF PATENT
APPEALS AND
INTERFERENCES

Appendix

Ex parte Rubin
Appeal 2001-1035
Application 08/835,482

Entries 1843, 3479 and 5490 from The Merck Index, CD-ROM, Version 12:1a, ISSN 1359-2947 (12th ed. 1996)

1843. Carbidopa.



S*-α-*Hydrazino-3,4-dihydroxy*-α-*methylbenzenepropanoic acid monohydrate; (-)*-L-α-*hydrazino-3,4-dihydroxy*-α-*methylhydrocinnamic acid monohydrate; α-hydrazino-α-methyl-β-(3,4-dihydroxyphenyl)propionic acid monohydrate; L-α-(3,4-dihydroxybenzyl)-α-hydrazinopropionic acid monohydrate; α-methyldopahydrazine; HMD; MK-486; Lodosin (Merck & Co.); Lodosyn (Merck & Co.). $C_{10}H_{14}N_2O_4.H_2O$; mol wt 244.25. C 49.18%, H 6.60%, N 11.47%, O 32.75%. Peripheral decarboxylase inhibitor. Prepn of DL-form: Pfister, **Fr.** pat. **M1553** (1962 to Merck & Co.), *C.A.* **59,** 12921e (1963); Sletzinger *et al., J. Med. Chem.* **6,** 101 (1963); **Brit.** pat. **940,596;** Chemerda *et al.,* **U.S.** pat. **3,462,536** (1963, 1969 both to Merck & Co.). Synthesis of the L-form: Karady *et al.,* **Ger.** pats. **2,062,285; 2,062, 332** (both 1971 to Merck & Co.), *C.A.* **75,** 118122t, 118120r (1971); *eidem, J. Org. Chem.* **36,** 1946, 1949 (1971). Inhibition of dopa decarboxylase: Porter *et al., Biochem. Pharmacol.* **11,** 1067 (1962); Moran, Sourkes, *J. Pharmacol. Exp. Ther.* **148,** 252 (1962); Watanabe *et al., Clin. Pharmacol. Ther.* **11,** 740 (1970). Only the L-form is pharmacologically active: Lotti, Porter, *J. Pharmacol. Exp. Ther.* **172,** 406 (1970).

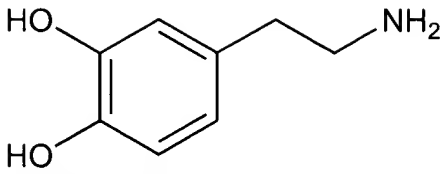
Crystals from hot water, mp 203-205° (dec). $[\alpha]_D$ -17.3° (methanol). Also reported as mp 208°.

Combination with levodopa, co-careldopa, Isicom (Isis), Nacom (Merck & Co.), Sinemet (Merck & Co.).

DL-Form, tan fluffy crystals, mp 206-208° (dec). uv max (methanol): 282.5 nm (ε 2940).

THERAP CAT: In combination with levodopa as antiparkinsonian.

3479. Dopamine.



4-(2-Aminoethyl)-1,2-benzenediol; 4-(2-aminoethyl)pyrocatechol; 3-hydroxytyramine; 3,4-dihydroxyphenethylamine; α-(3,4-dihydroxyphenyl)-β-aminoethane. $C_8H_{11}NO_2$; mol wt 153.18. C 62.73%, H 7.24%, N 9.14%, O 20.89%. Endogenous catecholamine with α and β-adrenergic activity. Isoln from *Hermidium alipes* (S. Watson) *Nyctaginaceae:* Buelow, Gisvold, *J. Am. Pharm. Assoc.* **33,** 270 (1944). Prepn from aminotyramine: Waser, Sommer, *Helv. Chim. Acta* **6,** 61 (1923). From homoveratrylamine: Schopf, Bayeler, *Ann.* **513,** 196 (1934); Hahn, Stiehl, *Ber.* **69,** 2640 (1936). Comprehensive description of the hydrochloride: J. E. Carter *et al., Anal. Profiles Drug Subs.* **11,** 257-272 (1982). Review of pharmacology and clinical efficacy in oliguria: J. F. Dasta, M. G. Kirby, *Pharmacotherapy* **6,** 304 (1986).

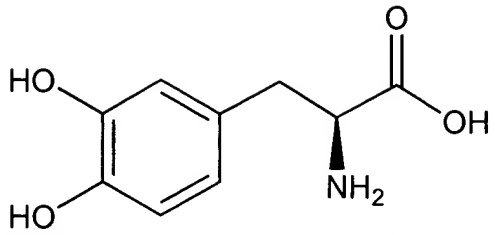
Free base, stout prisms, highly sensitive to oxygen; discolors quickly.

Hydrochloride, $C_8H_{11}NO_2$.HCl, ASL-279, Cardiosteril (Fresenius), Dopastat (Parke, Davis), Dynatra (Simes), Inovan (Kyowa), Inotropin (Bago). Rosettes of needles from water, dec 241°; may be recrystallized from methanol + ether. Freely sol in water; sol in methanol, in hot 95% ethanol; in aq solns of alkali hydroxides. Practically insol in ether, petr ether, chloroform, benzene, toluene.

Hydrobromide, $C_8H_{11}NO_2$.HBr, crystals, dec 210-214°.

THERAP CAT: Cardiotonic; antihypotensive.

5490. Levodopa.



3-Hydroxy-L-tyrosine; (-)-3-(3,4-dihydroxyphenyl)-L-alanine; L-dopa; β-(3,4-dihydroxyphenyl)-L-alanine; (-)-2-amino-3-(3,4-dihydroxyphenyl)propanoic acid; Bendopa (ICN); Deadopa (DeAngeli); Dopaflex (Medimpex); Dopal (Kyowa); Dopaidan (DeAngeli); Dopalina (Lepetit); Dopar; Doparkine (Armstrong); Doparl (Kyowa); Dopasol (Daiichi); Dopaston (Sankyo); Dopastral (Astra); Cidandopa (Cidán); Doprin (SK & F); Eldopal (Brocades-Stheeman); Eldopar (Weifa); Eldopatec (Labatec); Eurodopa (Europharma); Laradopa (Roche); Maipedopa (Maipe); Larodopa (Roche); Ledopa (Lepetit); Parda (Parke, Davis); Levopa (ICN); Veldopa (formerly Weldopa) (Smith & Nephew). $C_9H_{11}NO_4$; mol wt 197.19. C 54.82%, H 5.62%, N 7.10%, O 32.45%. Naturally occurring form of dopa, *q.v.*, the biological precursor of the catecholamines. Prepn from *l*-3-nitrotyrosin: Wasser, Lewandowski, *Helv. Chim. Acta* **4,** 657 (1921); from 3-(3,4-methylenedioxyphenyl)-L-alanine: Yamada *et al., Chem. Pharm. Bull.* **10,** 693 (1962); from L-tyrosine: Vorbruggen, Krolikiewicz, *Ber.* **105,** 1168 (1972); Bretschneider *et al., Helv. Chim. Acta* **56,** 2857 (1973); from *Vicia faba* beans: Wysong, **U.S.** pat. **3,253,023** (1966 to Dow Chem.); by fermentation of L-tyrosine: Sih *et al., J. Am. Chem. Soc.* **91,** 6204 (1969); Florent, Renaut, **Ger.** Offen. **2,102,793** (1971 to Rhone-Poulenc), *C.A.* **75,** 108505f (1971). Sepn from racemate: Vogler, Baumgartner, *Helv. Chim. Acta* **35,** 1776 (1952); **Neth.** pat. **Appl. 6,514, 950** corresp to **U.S.** pat. **3,405,159** (1966 and 1968 to Merck & Co.). Molecular conformation: Becker *et al., Biochem. Biophys. Res. Commun.* **41,** 444 (1970). Metabolism studies: Shaw *et al., J. Biol. Chem.* **226,** 255 (1957); Calne *et al., Brit. J. Pharmacol.* **37,** 57 (1969). Acute toxicity: *Rx Bulletin* **1,** 16 (November, 1970). Hemodynamic effects in congestive heart failure: S. I. Rajfer *et al., N. Engl. J. Med.* **310,** 1357 (1984). Series of articles on clinical efficacy in Parkinson's disease: *Advan. Neurol.* **45,** 457-510 (1986). Reviews on L-dopa and parkinsonism: Barbeau, *Can. Med. Assoc. J.* **101,** 791 (1969); Pletscher *et al., Schweiz. Med. Wochenschr.* **100,** 797 (1970); Calne, Sandler, *Nature* **226,** 21 (1970); *L-Dopa and Parkinsonism,* A. Barbeau, Ed. (F. A. Davis, Philadelphia, 1970). Comprehensive description: R. Gomez *et al., Anal. Profiles Drug Subs.* **5,** 189-223 (1976).

Colorless to white, odorless and tasteless crystals or crystalline powder. Needles from water, mp 276-278° (dec) (Yamada); also reported as mp 284-286° (Wysong). $[\alpha]_D^{13}$ -13.1° (c = 5.12 in 1*N* HCl). uv max (0.001*N* HCl): 220.5, 280 nm (log ε 3.79, 3.42). Readily sol in dil HCl and formic acid. Soly in water: 66 mg/40 ml. Practically insol in ethanol, benzene, chloroform and ethyl acetate. In the presence of moisture, L-dopa is rapidly oxidized by atmospheric oxygen and darkens. LD_{50} in mice, rats, rabbits (mg/kg): 3650, 4000, 609 orally (*Rx Bulletin).*

THERAP CAT: Antiparkinsonian.

cc (via First Class mail):

Gildo E. Fato, Esq.
515 Ash Street
Libertyville, IL 60048

Application Serial Number 08/835482

	DATE	INITIALS
Mail Personnel		
Receive case and PALM in	3-14-01	S.L.
Docket Personnel I		
OB/Heard Classification		
Outline case	3-20-01	
Reviewers		
Review/assign panel	6/4/01	
Prepare order/remand		
Docket Personnel I		
Enter data in ACTS/PALM		
Prep case (if panel assigned)		
Docket Personnel I		
Mail remand/order		
Administrators		
Assign Hearing Date		
Docket Personnel II		
Mail Notice of Hrg		
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BOARD OF PATENT APPEALS AND INTERFERENCES

DESIGNATION OF PANEL

Pursuant to (1) the Commissioner's authority to designate the members of the Board of Patent Appeals and Interferences to hear cases before the Board (35 U.S.C. 7(b)), and (2) Commissioner Lehman's memorandum dated May 1, 1994 (delegating to the Chief Administrative Patent Judge the responsibility of designating members to hear cases before the Board), it is ORDERED that the panel of the Board of Patent Appeals and Interferences designated to hear this case shall consist of the following members of the Board:

☐ On Brief ☐ Heard ☐ Redesignation ☐ Expanded Panel, see addendum.

1. Judge ~~William Smith~~ McKelvey
2. Judge ~~Hanks~~ William Smith
3. Judge ~~Grimes~~ Potate

Bruce H Stoner Jr

BRUCE H. STONER, JR.
Chief Administrative Patent Judge

Date of Hearing: _____